```
=> d his

     (FILE 'HOME' ENTERED AT 05:37:12 ON 28 NOV 2007)

     FILE 'REGISTRY' ENTERED AT 05:37:17 ON 28 NOV 2007
L1                STRUCTURE UPLOADED
L2              8 S L1
L3            267 S L1 SSS FULL

     FILE 'CAPLUS' ENTERED AT 05:38:00 ON 28 NOV 2007
L4              7 S L3
L5              0 S US200!-551933/ASPPS
L6              6 S US200!-551933/APPS
L7              1 S L4 AND L6
L8              6 S L4 NOT L7

     FILE 'REGISTRY' ENTERED AT 05:38:34 ON 28 NOV 2007

=> d l1
L1 HAS NO ANSWERS
L1                STR
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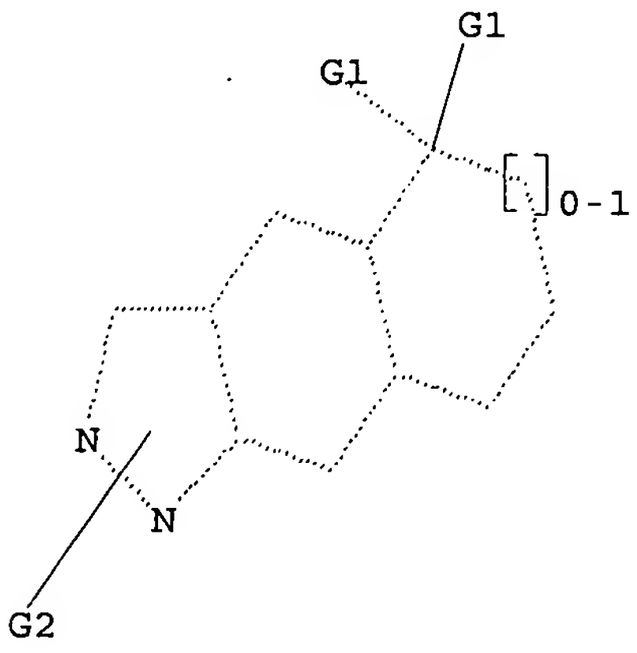


```
Cb 1
Hy 2
G1 C,O,S,N
G2 [@1],[@2]

Structure attributes must be viewed using STN Express query preparation.
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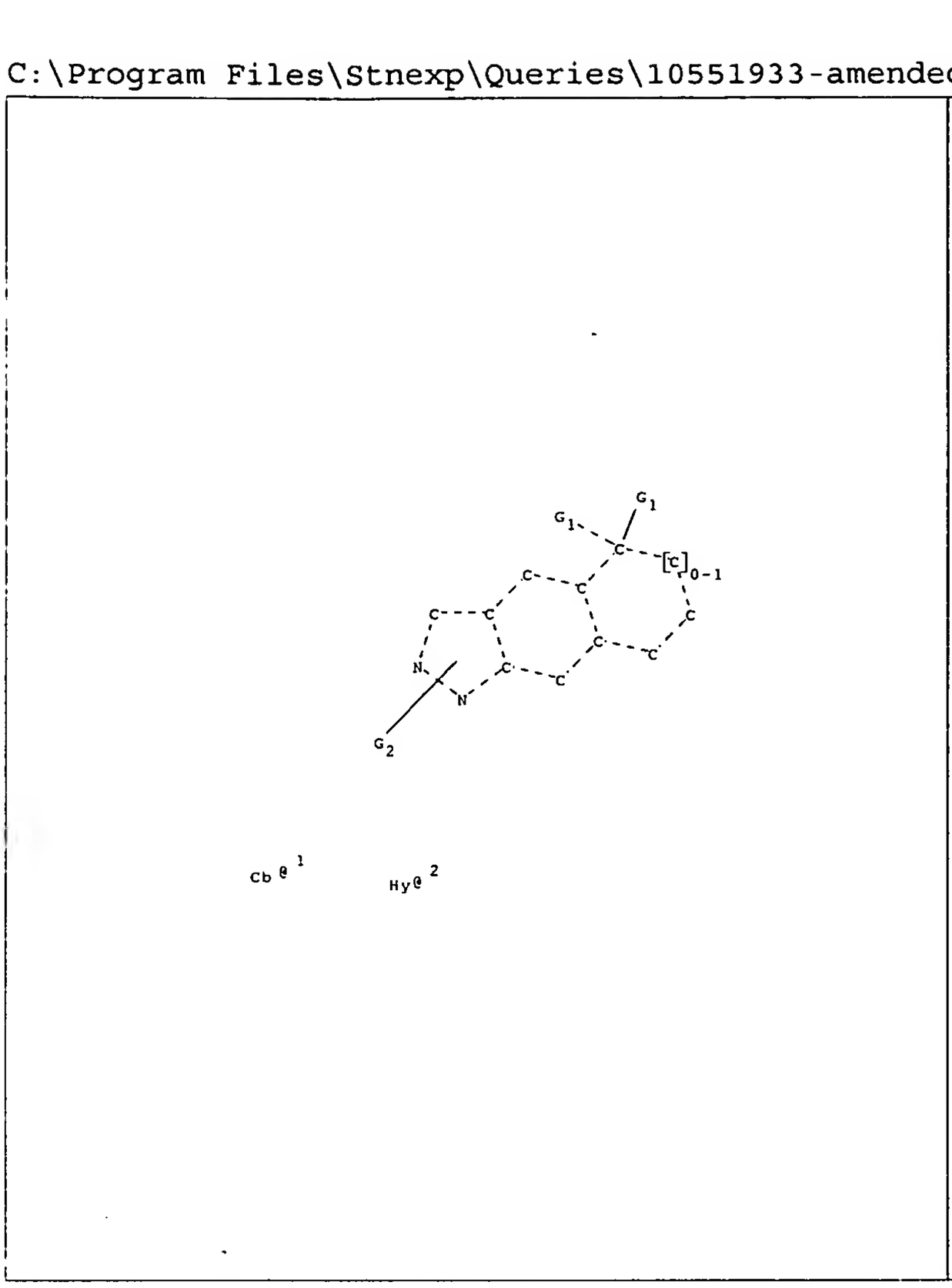
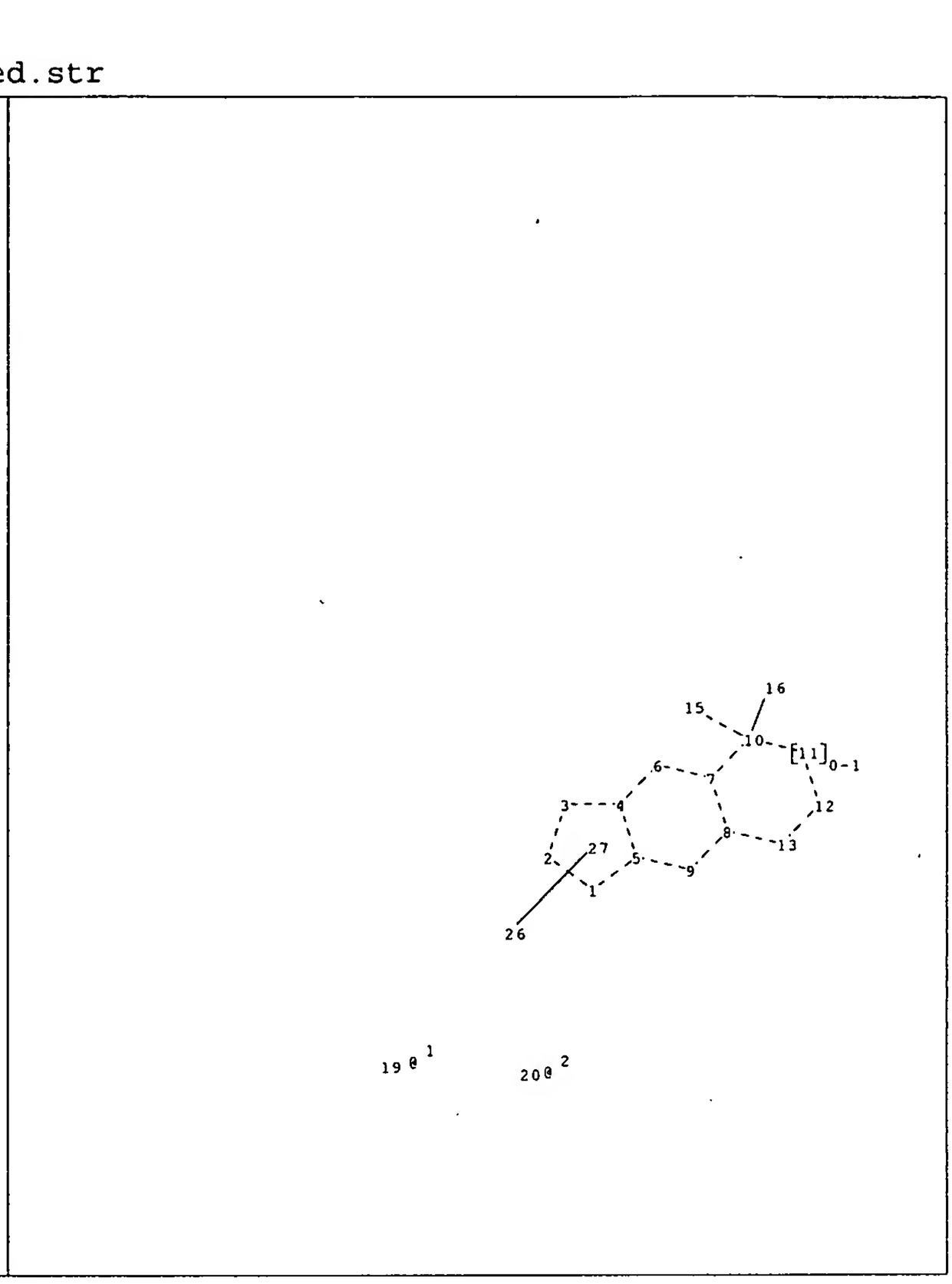
C:\Program Files\Stnexp\Queries\10551933-amended.str





chain nodes :
19 20 26
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 15 16
ring bonds :
1-2 1-5 2-3 3-4 4-5 4-6 5-9 6-7 7-8 7-10 8-9 8-13 10-11 10-15 10-16 11-12
12-13
exact/norm bonds :
1-2 1-5 2-3 3-4 4-5 4-6 5-9 6-7 7-8 7-10 8-9 8-13 10-11 10-15 10-16 11-12
12-13
isolated ring systems :
containing 1 :

G1:C,O,S,N

G2:[*1],[*2]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom
12:Atom 13:Atom 15:CLASS 16:CLASS 19:Atom 20:Atom 26:CLASS 27:CLASS
Generic attributes :
19:
Saturation : Unsaturated
Number of Carbon Atoms : less than 7
Type of Ring System : Monocyclic
20:

```
    Saturation              : Unsaturated
    Number of Carbon Atoms  : less than 7
    Number of Hetero Atoms  : Exactly 1
    Type of Ring System     : Monocyclic

Element Count :
    Node 19: Limited
        C,C6

    Node 20: Limited
        C,C5
        N,N1
```

L7 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:927012 CAPLUS
DN 141:395547
TI Preparation of selective spirocyclic glucocorticoid receptor modulators
IN Ali, Amjad; Balkovec, James M.; Beresis, Richard; Colletti, Steven L.; Graham, Donald W.; Patel, Gool F.; Smith, Cameron J.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 201 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

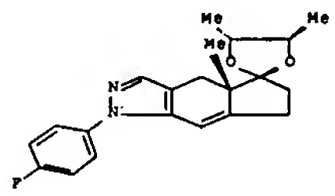
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004093805	A2	20041104	WO 2004-US12102	20040419
	WO 2004093805	A3	20051208		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2004232301	A1	20041104	AU 2004-232301	20040419
	CA 2522946	A1	20041104	CA 2004-2522946	20040419
	EP 1617806	A2	20060125	EP 2004-760029	20040419
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
	CN 1809347	A	20060726	CN 2004-80017051	20040419
	JP 2006524251	T	20061026	JP 2006-513140	20040419
	US 2006217563	A1	20060928	US 2005-551933	20051004 <--
	IN 2005DN04611	A	20070928	IN 2005-DN4611	20051010
PRAI	US 2003-464784P	P	20030423		
	WO 2004-US12102	W	20040419		

OS MARPAT 141:395547
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [Ring A = carbocyclyl or heterocyclyl; m = 0-3; n = 0-2; R1 = (un)substituted-alkyl, -alkenyl, -alkynyl, -cycloalkyl, etc.; R2 and R3 independently = H, halo, alkyl, aryl, etc.; R4 = OH, CO2H, (un)substituted-alkyl, -Ph, etc.] , as well as their pharmaceutically acceptable salts or hydrates thereof, are prepared and disclosed as selective glucocorticoid receptor ligands for treating a variety of autoimmune and inflammatory diseases or conditions. Thus, e.g., II was prepared via spirocyclization of III (preparation given) with Et α-bromomethyl acrylate. In human glucocorticoid receptor assays, I demonstrated a range of GR affinity with IC50 values between 10 μM and 1 nM. Pharmaceutical compns. and methods of use are also included.

L1 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:461153 CAPLUS Full-text
DN 143:125827
TI Novel ketal ligands for the glucocorticoid receptor: in vitro and in vivo activity
AU Smith, Cameron J.; Ali, Amjad; Balkovec, James M.; Graham, Donald W.; Hammond, Milton L.; Patel, Gool F.; Rouen, Gregory P.; Smith, Scott K.; Tata, James R.; Einstein, Monica; Ge, Lan; Harris, Georgianna S.; Kelly, Theresa M.; Mazur, Paul; Thompson, Chris M.; Wang, Chuanlin F.; Williamson, Joanne M.; Miller, Douglas K.; Pandit, Shilpa; Santoro, Joseph C.; Sitlani, Ayesha; Yamin, Ting-ting D.; O'Neill, Edward A.; Zaller, Dennis M.; Carballo-Jane, Ester; Forrest, Michael J.; Luell, Silvi
CS Department of Medicinal Chemistry, Merck Research Laboratories, Rahway, NJ, 07065, USA
SO Bioorganic & Medicinal Chemistry Letters (2005), 15(11), 2926-2931
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
OS CASREACT 143:125827
GI

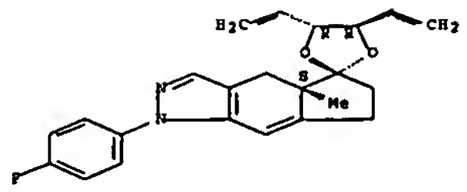


I

AB A novel series of selective ligands for the human glucocorticoid receptor is described. Structure-activity studies focused on variation of B-ring size, ketal ring size, and ketal substitution. These analogs were found to be potent and selective ligands for GR and have partial agonist profiles in functional assays for transactivation (TAT, GS) and transrepression (IL-6). Of these compds., three were evaluated further in a mouse LPS-induced TNF-α secretion model. Compound (I) had an ED50 of 14.1 mg/kg compared with 0.5 mg/kg for prednisolone in the same assay.

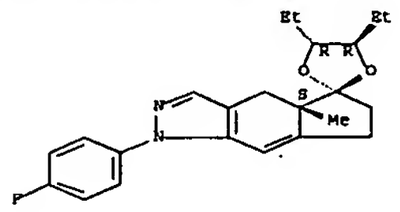
IT 786708-06-3
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(novel ketal ligands for glucocorticoid receptor and in vitro and in vivo activity)
RN 786708-06-3 CAPLUS
CN Spiro[cyclopent[f]indazole-5(1H),2'-[1,3]dioxolane], 4',5'-diethenyl-1-(4-fluorophenyl)-4,4a,6,7-tetrahydro-4a-methyl-, (4'R,4aS,5'R)- (CA INDEX NAME)

Absolute stereochemistry.



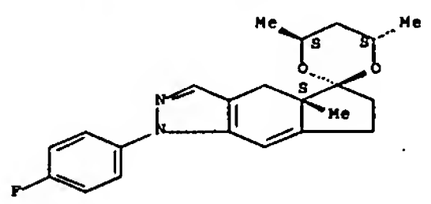
IT 786708-45-0P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(novel ketal ligands for glucocorticoid receptor and in vitro and in vivo activity)
RN 786708-45-0 CAPLUS
CN Spiro[cyclopent[f]indazole-5(1H),2'-[1,3]dioxolane], 4',5'-diethyl-1-(4-fluorophenyl)-4,4a,6,7-tetrahydro-4a-methyl-, stereoisomer (9CI) (CA INDEX NAME)

Absolute stereochemistry.



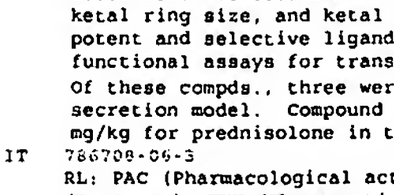
IT 786708-33-6
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel ketal ligands for glucocorticoid receptor and in vitro and in vivo activity)
RN 786708-33-6 CAPLUS
CN Spiro[cyclopent[f]indazole-5(1H),2'-[1,3]dioxane], 1-(4-fluorophenyl)-4,4a,6,7-tetrahydro-4',4a,6'-trimethyl-, (4'S,4aS,6'S)- (CA INDEX NAME)

Absolute stereochemistry.



IT 614762-99-1P 786707-55-9P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(novel ketal ligands for glucocorticoid receptor and in vitro and in vivo activity)
RN 614762-99-1 CAPLUS
CN Spiro[5H-benz[f]indazole-5,2'-[1,3]dioxolane], 1-(4-fluorophenyl)-1,4,4a,6,7,8-hexahydro-4a-methyl-, (4aS)- (CA INDEX NAME)

Absolute stereochemistry.

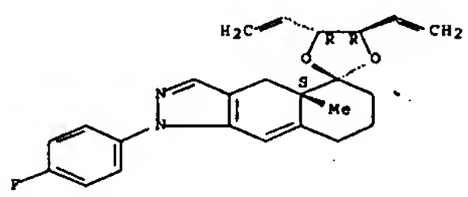


RN 786707-55-9 CAPLUS
CN Spiro[cyclopent[f]indazole-5(1H),2'-[1,3]dioxolane], 1-(4-fluorophenyl)-4,4a,6,7-tetrahydro-4a-methyl-, (4aS)- (CA INDEX NAME)

Absolute stereochemistry.

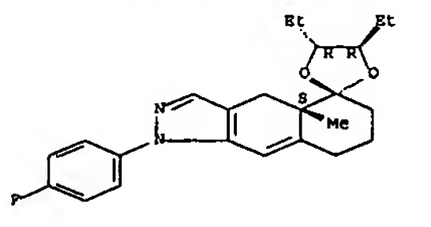
IT 786707-70-8
RL: PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(novel ketal ligands for glucocorticoid receptor and in vitro and in vivo activity)
RN 786707-70-8 CAPLUS
CN Spiro[5H-benz[f]indazole-5,2'-[1,3]dioxolane], 4',5'-diethenyl-1-(4-fluorophenyl)-1,4,4a,6,7,8-hexahydro-4a-methyl-, (4'R,4aS,5'R)- (CA INDEX NAME)

Absolute stereochemistry.



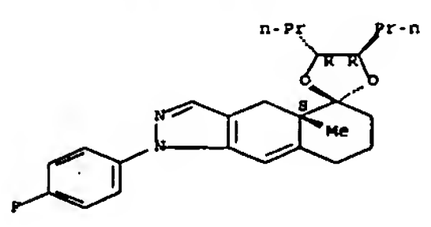
IT 786707-65-1P 786707-67-3P 786707-68-4P
558371-49-0P 558371-51-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(novel ketal ligands for glucocorticoid receptor and in vitro and in vivo activity)
RN 786707-65-1 CAPLUS
CN Spiro[5H-benz[f]indazole-5,2'-[1,3]dioxolane], 4',5'-diethyl-1-(4-fluorophenyl)-1,4,4a,6,7,8-hexahydro-4a-methyl-, (4'R,4aS,5'R)- (CA INDEX NAME)

Absolute stereochemistry.



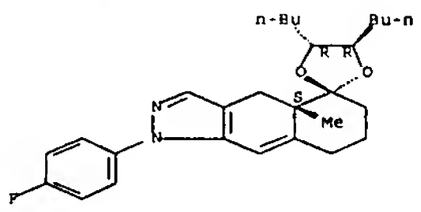
RN 786707-67-3 CAPLUS
CN Spiro[5H-benz[f]indazole-5,2'-[1,3]dioxolane], 1-(4-fluorophenyl)-1,4,4a,6,7,8-hexahydro-4a-methyl-4',5'-dipropyl-, (4'R,4aS,5'R)- (CA INDEX NAME)

Absolute stereochemistry.



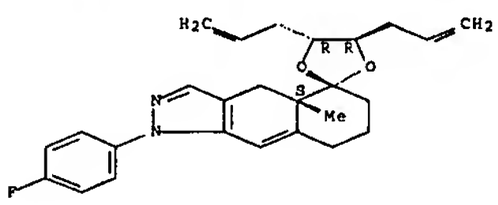
RN 786707-68-4 CAPLUS
CN Spiro[5H-benz[f]indazole-5,2'-[1,3]dioxolane], 4',5'-dibutyl-1-(4-fluorophenyl)-1,4,4a,6,7,8-hexahydro-4a-methyl-, (4'R,4aS,5'R)- (CA INDEX NAME)

Absolute stereochemistry.



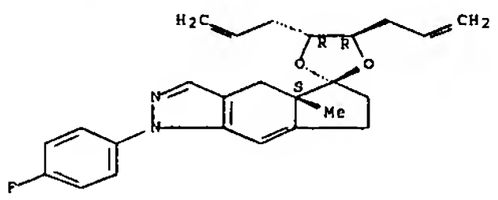
RN 858371-49-0 CAPLUS
CN Spiro[5H-benz[f]indazole-5,2'-[1,3]dioxolane], 1-(4-fluorophenyl)-1,4,4a,6,7,8-hexahydro-4a-methyl-4',5'-di-2-propenyl-, (4'R,4aS,5'R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 858371-51-4 CAPLUS
CN Spiro[cyclopent[f]indazole-5(1H),2'-[1,3]dioxolane], 1-(4-fluorophenyl)-4,4a,6,7-tetrahydro-4a-methyl-4',5'-di-2-propenyl-, (4'R,4aS,5'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 786707-63-9 786709-10-9 786708-11-0
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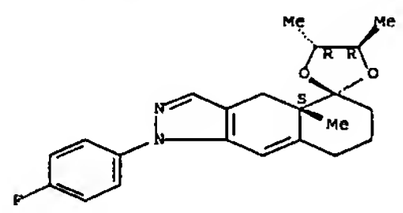
786708-20-1 786708-21-2 786708-34-7
786708-36-9 787619-93-6 787620-00-3
787620-02-4 787620-09-1 787620-10-4
858371-54-7 858371-55-8 858371-57-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel ketal ligands for glucocorticoid receptor and in vitro and in vivo activity)

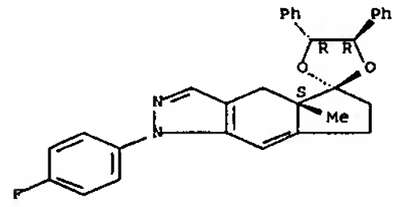
RN 786707-63-9 CAPLUS
CN Spiro[5H-benz[f]indazole-5,2'-[1,3]dioxolane], 1-(4-fluorophenyl)-1,4,4a,6,7,8-hexahydro-4',4a,5'-trimethyl-, (4'R,4aS,5'R)- (CA INDEX NAME)

Absolute stereochemistry.



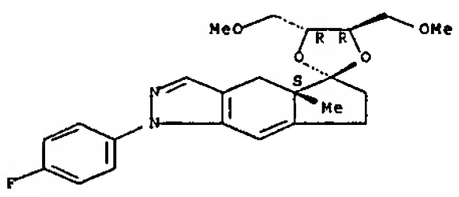
RN 786708-10-9 CAPLUS
CN Spiro[cyclopent[f]indazole-5(1H),2'-[1,3]dioxolane], 1-(4-fluorophenyl)-4,4a,6,7-tetrahydro-4a-methyl-4',5'-diphenyl-, (4'R,4aS,5'R)- (CA INDEX NAME)

Absolute stereochemistry.



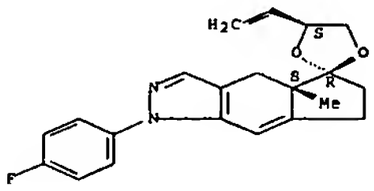
RN 786708-11-0 CAPLUS
CN Spiro[cyclopent[f]indazole-5(1H),2'-[1,3]dioxolane], 1-(4-fluorophenyl)-4,4a,6,7-tetrahydro-4',5'-bis(methoxymethyl)-4a-methyl-, (4'R,4aS,5'R)-(CA INDEX NAME)

Absolute stereochemistry.



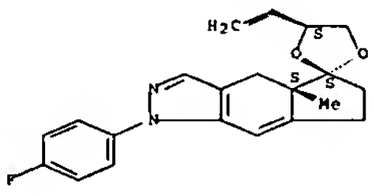
RN 786708-14-3 CAPLUS
CN Spiro[cyclopent[f]indazole-5(1H),2'-[1,3]dioxolane], 4'-ethenyl-1-(4-fluorophenyl)-4,4a,6,7-tetrahydro-4a-methyl-, (2'R,4'S,4aS)- (CA INDEX NAME)

Absolute stereochemistry.



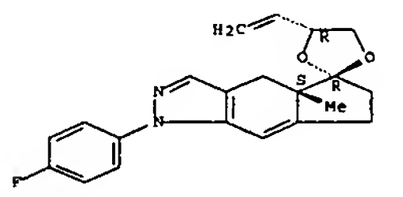
RN 786708-15-4 CAPLUS
CN Spiro[cyclopent[f]indazole-5(1H),2'-[1,3]dioxolane], 4'-ethenyl-1-(4-fluorophenyl)-4,4a,6,7-tetrahydro-4a-methyl-, (2'S,4'S,4aS)- (CA INDEX NAME)

Absolute stereochemistry.



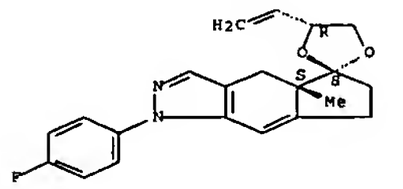
RN 786708-16-5 CAPLUS
CN Spiro[cyclopent[f]indazole-5(1H),2'-[1,3]dioxolane], 4'-ethenyl-1-(4-fluorophenyl)-4,4a,6,7-tetrahydro-4a-methyl-, (2'R,4'R,4aS)- (CA INDEX NAME)

Absolute stereochemistry.



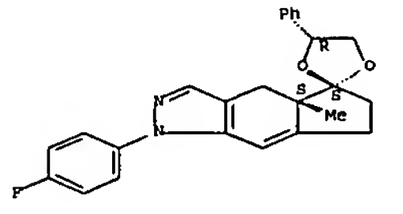
RN 786708-17-6 CAPLUS
CN Spiro[cyclopent[f]indazole-5(1H),2'-[1,3]dioxolane], 4'-ethenyl-1-(4-fluorophenyl)-4,4a,6,7-tetrahydro-4a-methyl-, (2'S,4'R,4aS)- (CA INDEX NAME)

Absolute stereochemistry.



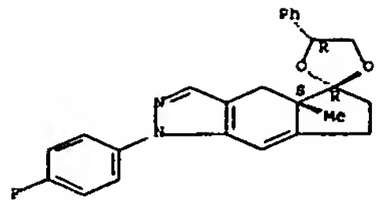
RN 786708-18-7 CAPLUS
CN Spiro[cyclopent[f]indazole-5(1H),2'-[1,3]dioxolane], 1-(4-fluorophenyl)-4,4a,6,7-tetrahydro-4a-methyl-4'-phenyl-, (2'S,4'R,4aS)- (CA INDEX NAME)

Absolute stereochemistry.



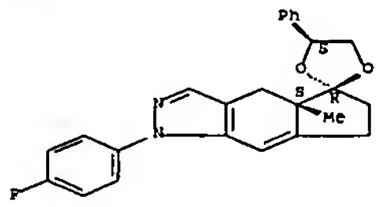
RN 786708-19-8 CAPLUS
CN Spiro[cyclopent[f]indazole-5(1H),2'-[1,3]dioxolane], 1-(4-fluorophenyl)-4,4a,6,7-tetrahydro-4a-methyl-4'-phenyl-, (2'R,4'R,4aS)- (CA INDEX NAME)

Absolute stereochemistry.



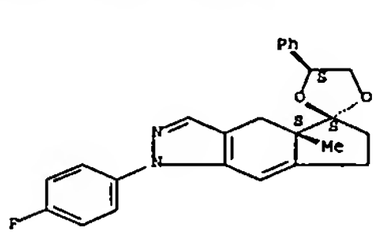
RN 786708-20-1 CAPLUS
CN Spiro[cyclopent[f]indazole-5(1H),2'-[1,3]dioxolane], 1-(4-fluorophenyl)-4,4a,6,7-tetrahydro-4a-methyl-4'-phenyl-, (2'R,4'S,4aS)- (CA INDEX NAME)

Absolute stereochemistry.



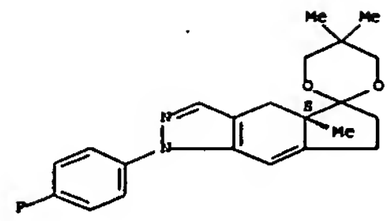
RN 786708-21-2 CAPLUS
CN Spiro[cyclopent[f]indazole-5(1H),2'-[1,3]dioxolane], 1-(4-fluorophenyl)-4,4a,6,7-tetrahydro-4a-methyl-4'-phenyl-, (2'S,4'S,4aS)- (CA INDEX NAME)

Absolute stereochemistry.



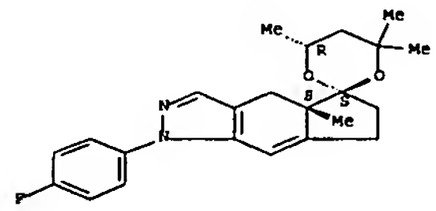
RN 786708-34-7 CAPLUS
CN Spiro[cyclopent[f]indazole-5(1H),2'-[1,3]dioxane], 1-(4-fluorophenyl)-4,4a,6,7-tetrahydro-4a,5',5'-trimethyl-, (4aS)- (CA INDEX NAME)

Absolute stereochemistry.



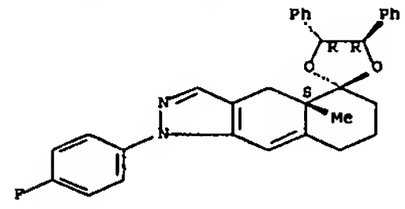
RN 786708-36-9 CAPLUS
CN Spiro[cyclopent[f]indazole-5(1H),2'-[1,3]dioxane], 1-(4-fluorophenyl)-4,4a,6,7-tetrahydro-4',4',4a,6'-tetramethyl-, (2'S,4aS,6'R)- (CA INDEX NAME)

Absolute stereochemistry.



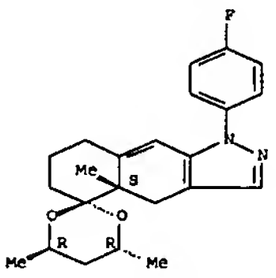
RN 787619-93-6 CAPLUS
CN Spiro[5H-benz[f]indazole-5,2'-[1,3]dioxolane], 1-(4-fluorophenyl)-1,4,4a,6,7,8-hexahydro-4a-methyl-4',5'-diphenyl-, (4'R,4aS,5'R)- (CA INDEX NAME)

Absolute stereochemistry.



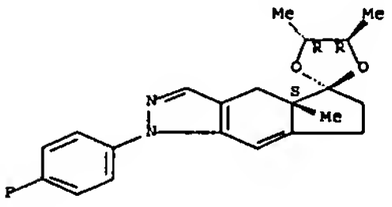
RN 787620-00-2 CAPLUS
CN Spiro[5H-benz[f]indazole-5,2'-[1,3]dioxane], 1-(4-fluorophenyl)-1,4,4a,6,7,8-hexahydro-4',4a,6'-trimethyl-, (4'R,4aS,6'R)- (CA INDEX NAME)

Absolute stereochemistry.



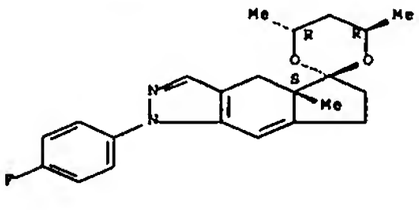
RN 787620-02-4 CAPLUS
CN Spiro[cyclopent[f]indazole-5(1H),2'-[1,3]dioxolane], 1-(4-fluorophenyl)-4,4a,6,7-tetrahydro-4',4a,5'-trimethyl-, (4'R,4aS,5'R)- (CA INDEX NAME)

Absolute stereochemistry.



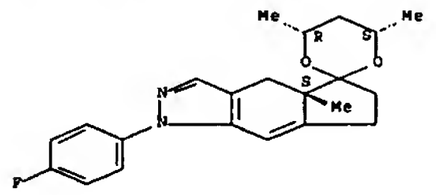
RN 787620-09-1 CAPLUS
CN Spiro[cyclopent[f]indazole-5(1H),2'-[1,3]dioxane], 1-(4-fluorophenyl)-4,4a,6,7-tetrahydro-4',4a,6'-trimethyl-, (4'R,4aS,6'R)- (CA INDEX NAME)

Absolute stereochemistry.



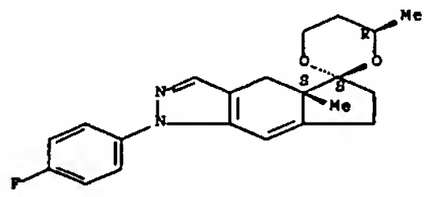
RN 787620-10-4 CAPLUS
CN Spiro[cyclopent[f]indazole-5(1H),2'-[1,3]dioxane], 1-(4-fluorophenyl)-4,4a,6,7-tetrahydro-4',4a,6'-trimethyl-, (4'R,4aS,6'S)- (CA INDEX NAME)

Absolute stereochemistry.



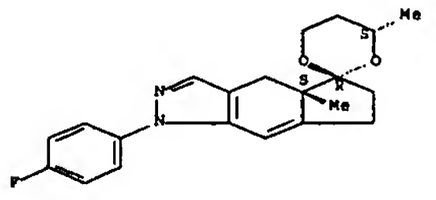
RN 858371-54-7 CAPLUS
CN Spiro[cyclopent[f]indazole-5(1H),2'-[1,3]dioxane], 1-(4-fluorophenyl)-4,4a,6,7-tetrahydro-4',4a-dimethyl-, (2'S,4'R,4aS)- (CA INDEX NAME)

Absolute stereochemistry.



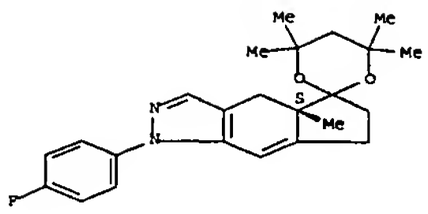
RN 858371-55-8 CAPLUS
CN Spiro[cyclopent[f]indazole-5(1H),2'-[1,3]dioxane], 1-(4-fluorophenyl)-4,4a,6,7-tetrahydro-4',4a-dimethyl-, (2'R,4'S,4aS)- (CA INDEX NAME)

Absolute stereochemistry.



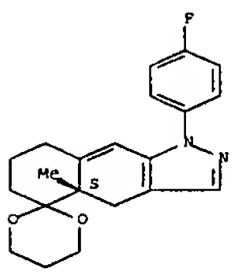
RN 858371-57-0 CAPLUS
CN Spiro[cyclopent[f]indazole-5(1H),2'-[1,3]dioxane], 1-(4-fluorophenyl)-4,4a,6,7-tetrahydro-4',4',4a,6',6'-pentamethyl-, (4aS)- (CA INDEX NAME)

Absolute stereochemistry.



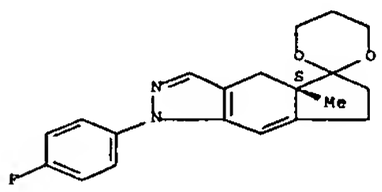
IT 786708-00-7P 786708-30-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(novel ketal ligands for glucocorticoid receptor and in vitro and in vivo activity)
RN 786708-00-7 CAPLUS
CN Spiro[5H-benz[f]indazole-5,2'-[1,3]dioxane], 1-(4-fluorophenyl)-1,4,4a,6,7,8-hexahydro-4a-methyl-, (4aS)- (CA INDEX NAME)

Absolute stereochemistry.



RN 786708-30-3 CAPLUS
CN Spiro[cyclopent[f]indazole-5(1H),2'-[1,3]dioxane], 1-(4-fluorophenyl)-4,4a,6,7-tetrahydro-4a-methyl-, (4aS)- (CA INDEX NAME)

Absolute stereochemistry.

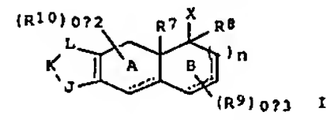


RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:740124 CAPLUS Full-text
DN 141:260743
TI Preparation of cyclopent[f]indazole and benz[f]indazole derivatives selective non-steroidal glucocorticoid receptor modulators
IN Ali, Amjad; Beresis, Richard; Colletti, Steven L.; Graham, Donald W.; Tata, James R.; Thompson, Christopher F.
PA Merck & Co. Inc., USA
SO PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004075840	A2	20040910	WO 2004-US5199	20040220
WO 2004075840	A3	20050203		
WO 2004075840	A9	20050804		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004216182	A1	20040910	AU 2004-216182	20040220
CA 2516684	A1	20040910	CA 2004-2516684	20040220
EP 1599201	A2	20051130	EP 2004-713398	20040220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006518752	T	20060817	JP 2006-503780	20040220
US 2006074120	A1	20060406	US 2005-544899	20050808
PRAI US 2003-450811P	P	20030225		
WO 2004-US5199	W	20040220		

OS MARPAT 141:260743
GI



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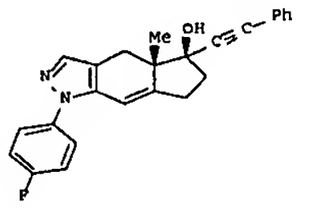
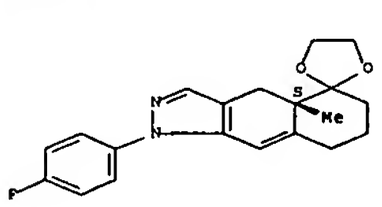


II

AB Title compds. represented by the formula I [wherein J = NR1, CR1R2; K = NR3, CR3R4; L = NR5, CR5R6; X = hydroxy, alkoxy, carbamoyl, etc.; R1-R6 = independently H, halo, (cyclo)alkyl, etc.; R7 = H, hydroxy, alkoxy, aryl, etc.; R8 = (cyclo)alkyl, alkenyl, alkynyl, etc.; R9, R10 = independently halo, hydroxy, alkyl, alkenyl, alkoxy; n = 0-2; and pharmaceutically acceptable salts or hydrates thereof] were prepared as selective non-steroidal glucocorticoid receptor modulators. For example, II was given in a multi-steps synthesis starting from 1-(4-fluorophenyl)-4,4a,6,7- tetrahydro-4a-methyl-cyclopent[f]indazol-5(1H)-one reacting with phenylethynylmagnesium bromide. I showed affinity of glucocorticoid receptor with IC50 values between 10 μM and 1 nM. Thus, I and their pharmaceutical compns. are useful for the treatment of a variety of autoimmune and inflammatory diseases or conditions.
IT 614762-99-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of cyclopent[f]indazol-5-yl and benz[f]indazol-5-yl derivs. as selective non-steroidal glucocorticoid receptor modulators)
RN 614762-99-1 CAPLUS
CN Spiro[5H-benz[f]indazole-5,2'-[1,3]dioxolane], 1-(4-fluorophenyl)-1,4,4a,6,7,8-hexahydro-4a-methyl-, (4aS)- (CA INDEX NAME)

Absolute stereochemistry.



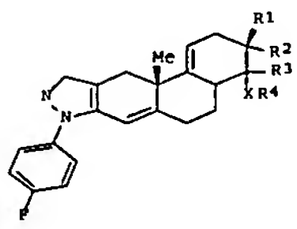
intermediate

L2 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:270010 CAPLUS Full-text
DN 140:287380
TI Preparation of octahydro-2-H-naphtho[1,2-f]indole-4-carboxamide derivatives as selective glucocorticoid receptor modulators for the treatment of autoimmune and inflammatory conditions
IN Ali, Amjad; Aster, Susan D.; Balkovec, James M.; Graham, Donald W.; Hunt, Julianne A.; Kallashi, Florida; Sinclair, Peter J.; Tata, James R.; Taylor, Gayle E.; Goulet, Joung L.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 170 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004026248	A2	20040401	WO 2003-US29494	20030917

WO 2004026248	A3	20040715		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2499150	A1	20040401	CA 2003-2499150	20030917
AU 2003270783	A1	20040408	AU 2003-270783	20030917
EP 1542996	A2	20050622	EP 2003-752495	20030917
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006503107	T	20060126	JP 2004-568945	20030917
US 2005245588	A1	20051103	US 2005-527615	20050311
PRAI US 2002-412231P	P	20020920		
US 2003-476079P	P	20030605		
WO 2003-US29494	W	20030917		

OS MARPAT 140:287380
GI



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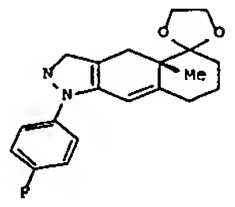


II

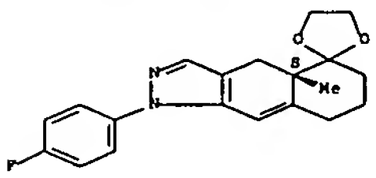
AB Octahydro-2-H-naphtho[1,2-f]indole-4-carboxamide derivs. I (X = CO, NHCO, CONH, NH, CH2NH; R1,R2 = H, alkyl, alkenyl, cycloalkyl, alkoxy, aryl; R3 = alkyl, alkoxy, acid, halogen substituted alkyl; R4 = alkyl, alkenyl, cycloalkoxy, alkoxy, aryl) were prepared as selective glucocorticoid receptor modulators for the treatment of autoimmune and inflammatory conditions. Thus, (S)-Wieland-Miescher ketone was protected as the ketal using p-toluene sulfonic acid and ethylene glyclol and then treated with Et formate to give the hydroxymethylene ketal derivative The hydroxymethylene was dissolved in acetic acid and reacted with p-fluorophenyl hydrazine hydrochloride to give II. The ketal of II was converted to the ketone using 6N HCl, and the resulting ketone transformed into the triflate. The triflate was treated with tributylvinyl tin and PPh3 to give the corresponding coupling product. Treatment with ethyl-4,4,4- trifluorocrotonate followed by dropwise addition of BCl3 gave the target I (R1 = CF3, R2, R3 = H, X = CO, R4 = OEt),.
IT 614762-99-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of octahydronaphthoindole-4-carboxamide derivs. as selective glucocorticoid receptor modulators for the treatment of autoimmune and inflammatory conditions)

RN 614762-99-1 CAPLUS

CN Spiro[5H-benz[f]indazole-5,2'-[1,3]dioxolane], 1-(4-fluorophenyl)-1,4,4a,6,7,8-hexahydro-4a-methyl-, (4aS)- (CA INDEX NAME)

Absolute stereochemistry.



intermediate

L8 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:267662 CAPLUS Full-text

DN 141:7063

TI Novel N-Arylpyrazolo[3,2-c]-Based Ligands for the Glucocorticoid Receptor: Receptor Binding and in Vivo Activity

AU Ali, Amjad; Thompson, Christopher F.; Balkovec, James M.; Graham, Donald W.; Hammond, Milton L.; Quraishi, Nazia; Tata, James R.; Einstein, Monica; Ge, Lan; Harris, Georgianna; Kelly, Terri M.; Mazur, Paul; Pandit, Shilpa; Santoro, Joseph; Sitlani, Ayesha; Wang, Chuanlin; Williamson, Joanne; Miller, Douglas K.; Thompson, Chris M.; Zaller, Dennis M.; Forrest, Michael J.; Carballo-Jane, Ester; Luell, Silvi

CS Departments of Medicinal Chemistry, Metabolic Disorders Immunonology and Pharmacology, Merck Research Laboratories, Rahway, NJ, 07065, USA

SO Journal of Medicinal Chemistry (2004), 47(10), 2441-2452
CODEN: JMCMAR; ISSN: 0022-2623

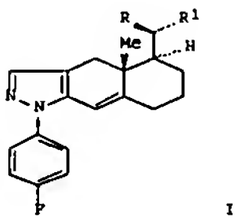
PB American Chemical Society

DT Journal

LA English

OS CASREACT 141:7063

GI



I

AB A novel series of selective ligands for the human glucocorticoid receptor (hGR) are described. Preliminary structure-activity relationships were focused on substitution at C-1 and indicated a preference for 3-, 4-, and 5-substituted aromatic and benzylic groups. The resulting analogs, e.g., I [R = OH, R1 = 3,4,5-MeO(F2)C6H2, CH2C6H4F-4], exhibited excellent affinity for hGR (IC50 1.9 nM and 2.8 nM, resp.) and an interesting partial agonist profile in functional assays of transactivation (tyrosine aminotransferase, TAT, and glutamine synthetase, GS) and transrepression (IL-6). The most potent compds. were I [R = 4-FC6H4, 2-thienyl, R1 = OH]. These candidates showed highly efficacious IL-6 inhibition vs. dexamethasone. I [R = 2-thienyl, R1 = OH] was evaluated in vivo in the mouse LPS challenge model and showed an ED50 = 4.0 mg/kg, compared to 0.5 mg/kg for prednisolone in the same assay.

IT 614762-99-1P

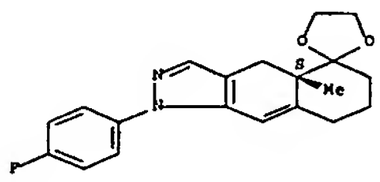
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and glucocorticoid receptor binding of [aryl(hydroxy)methyl]naphthopyrazoles)

RN 614762-99-1 CAPLUS

CN Spiro[5H-benz[f]indazole-5,2'-[1,3]dioxolane], 1-(4-fluorophenyl)-1,4,4a,6,7,8-hexahydro-4a-methyl-, (4aS)- (CA INDEX NAME)

Absolute stereochemistry.



intermediate

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2003:836773 CAPLUS Full-text

DN 139:323524

TI Preparation of 1H-Benzo[f]indazol-5-yl derivatives as selective glucocorticoid receptor modulators

IN Ali, Amjad; Balkovec, James M.; Graham, Donald W.; Thompson, Christopher F.; Quraishi, Nazia

PA Merck & Co., Inc., USA

SO PCT Int. Appl., 233 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003086294	A2	20031023	WO 2003-US10867	20030408
WO 2003086294	A3	20040715		

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PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

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CA 2481320	A1	20031023	CA 2003-2481320	20030408
AU 2003221706	A1	20031027	AU 2003-221706	20030408
EP 1496892	A2	20050119	EP 2003-718285	20030408

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

JP 2005528385	T	20050922	JP 2003-583721	20030408
US 2005256315	A1	20051117	US 2005-508897	20050428
US 7282591	B2	20071016		
PRAI US 2002-371948P	P	20020411		
WO 2003-US10867	W	20030408		

OS MARPAT 139:323524

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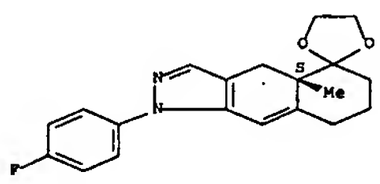
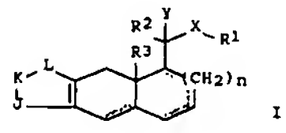
receptor modulators)

RN 614762-99-1 CAPLUS

CN Spiro[5H-benz[f]indazole-5,2'-[1,3]dioxolane], 1-(4-fluorophenyl)-1,4,4a,6,7,8-hexahydro-4a-methyl-, (4aS)- (CA INDEX NAME)

Absolute stereochemistry.





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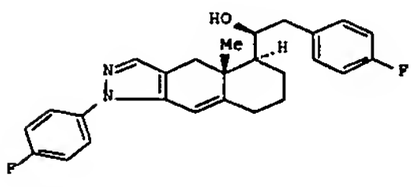


II

AB Benzindazoles I [n = 0-2; J, K, L = (un)substituted CH2, NH; X = bond, CO, (un)substituted NH, NHCO, 1,1-cyclopropanediyl; R1, R2 = H, (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, aryl, aralkyl, heterocyclic, aryloxy, aroyloxy, OH; R3 = H, (un)substituted OH, alkyl, aryl, aralkyl; Y = H, (un)substituted OH, SH, S(O)H, SO2H, CH2, NH2, SO2NH2, CO2H, NO2, acyl, CN, halogen; and the carbocyclic rings may be further substituted] were prepared for use as selective glucocorticoid receptor ligands for treating a variety of autoimmune and inflammatory diseases or conditions (no data). Thus, Wieland-Miescher ketone was ketalized, hydroxymethylenated, cyclized with 4-FC6H4NHNH2, deketalized, treated with Ph3P+CH2OMe Cl-, and subjected to Grignard reaction with 4-FC6H4MgCl to give the benzindazole II.

IT 614762-99-1P 614763-23-4P

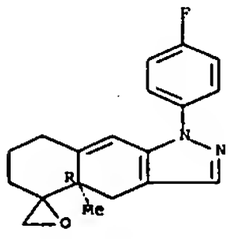
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 1H-benzo[f]indazol-5-yl derivs. as selective glucocorticoid

RN 614763-23-4 CAPLUS

CN Spiro[5H-benz[f]indazole-5,2'-oxirane], 1-(4-fluorophenyl)-1,4,4a,6,7,8-hexahydro-4a-methyl-, (4aR)- (CA INDEX NAME)

Absolute stereochemistry.



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L8 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2003:590999 CAPLUS Full-text

DN 139:149523

TI Preparation of non-steroidal ligands for the glucocorticoid receptor

IN Scanlan, Thomas S.; Shah, Nilesh

PA The Regents of the University of California, USA

SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003061651	A1	20030731	WO 2003-US1997	20030122

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- no alternative of actual synthesis (ie of something that could be drug like) - no motivation b/c it's only intermediate

UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2473886	A1	20030731	CA 2003-2473886	20030122
US 2003176478	A1	20030918	US 2003-350260	20030122
US 6831093	B2	20041214		
EP 1467730	A1	20041020	EP 2003-710722	20030122
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JP 2005523254	T	20050804	JP 2003-561595	20030122
US 2005054700	A1	20050310	US 2004-972250	20041022
PRAI US 2002-351484P	P	20020122		
US 2002-373757P	P	20020417		
US 2003-350260	A3	20030122		
WO 2003-US1997	W	20030122		

OS MARPAT 139:149523
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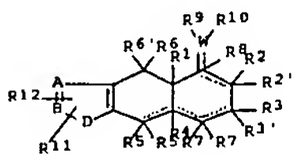

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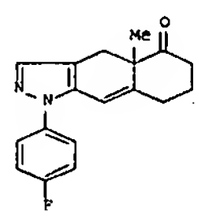


II

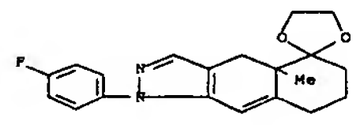
AB Naphthoheterocycles I [A, B, D = C, N, O, S, at least one of A, B, and D being N, O, or S; W = C, O, N, S; R1 = H, (un)substituted alkyl, acyl, NH2, CO2H, aralkyl, CONH2, heterocyclic, CN, halogen; R2, R3, R5, R6, R6', R7 = H, (un)substituted alkyl, acyl, alkoxy, NH2, sulfonyl, sulfinyl, SH, CO2H, aralkyl, CONH2, heterocyclic, OH, CN, halogen; R2', R3', R5', R7', R8 = absent or H, (un)substituted alkyl, acyl, NH2, alkoxy, sulfonyl, sulfinyl, SH, aralkyl, CONH2, heterocyclic, CN, halogen; R4 = absent or H, (un)substituted alkyl, acyl, NH2, CO2H, aralkyl, CONH2, heterocyclic, CN, halogen; R9 = absent or H, (un)substituted alkyl, alkoxy, NH2, CO2H, CN, halogen, O, S, OH; R10 = absent or H, (un)substituted alkyl, acyl, CO2H, aralkyl, aryl, cycloalkyl, heterocyclic; R2R10 = atoms required to form a ring; R11, R12 = H, (un)substituted alkyl, acyl, NH2, alkoxy, sulfonyl, sulfinyl, SH, aryl, aralkyl, CONH2, heterocyclic, OH, CN, halogen, O, S] were prepared as non-steroidal ligands for the glucocorticoid receptor. They are useful for treating or preventing diseases (e.g., obesity, diabetes, depression, neurodegeneration of an inflammatory disease) associated with glucocorticoid binding to the glucocorticoid receptor. Thus, Wieland-Miescher ketone was

converted to its 5-ethyleneketal, hydroxymethylenated, and cyclized with 4-FC6H4NHNH2 to give the benzindazolone II which had IC50 of 436 nM in a glucocorticoid receptor binding test.

IT 571203-14-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of non-steroidal ligands for the glucocorticoid receptor)

RN 571203-14-0 CAPLUS

CN Spiro[5H-benz[f]indazole-5,2'-[1,3]dioxolane], 1-(4-fluorophenyl)-1,4,4a,6,7,8-hexahydro-4a-methyl- (CA INDEX NAME)



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	34.92	212.17
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-5.46	-5.46

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 05:39:23 ON 28 NOV 2007